

Suppl. Table 1: ONCOKB levels of evidence (adapted from ONCOKB)

1	FDA-recognized biomarker for an FDA-approved drug in that indication
2a	Standard of care biomarker for an FDA-approved drug in that indication
2b	Standard of care biomarker for an FDA-approved drug in a different indication
3a	Compelling evidence for efficacy of the biomarker in predicting response to a drug in that indication
3b	Compelling evidence for efficacy of the biomarker in predicting response to a drug in a different indication
4	Preclinical evidence for efficacy of drug against a particular alteration
R1	Alterations that proved to imply resistance to a treatment

Supplementary Table 2: patients characteristics

Characteristics	ttNGS (n=186)	lbNGS (n=46)
<b>Age</b>		
Median	61	64
Range	18-78	38-87
<b>Sex</b>		
Male	85 (45,7%)	21 (45,6%)
Female	101 (54,3%)	25 (54,3%)
<b>Samples Analysed</b>		
1	178 (95,7%)	40 (86,9%)
2	7 (3,8%)	5 (10,7%)
3	1 (0,5%)	1 (2,2%)
<b>Tumor type</b>		
Adrenal gland	2	-
Breast	13	-
Cervix	2	-
Cholangiocarcinoma	7	2
Colorectal Adenocarcinoma	26	6
Esophagus	6	-
Gallbladder	2	-
Head & Neck	2	-
Kidney	5	-
Liver	6	-
Lung	37	19
<i>adenocarcinoma</i>	20	11
<i>squamous cell carcinoma</i>	4	3
<i>SCLC</i>	8	3
<i>other lung cancer</i>	5	2
Mesothelioma	7	-
Occult	3	-
Ovary	10	-
Pancreatic Adenocarcinoma	22	5
Prostate Adenocarcinoma	4	4
Salivary Gland	5	-
Stomach	3	-
Soft Tissue Sarcoma	6	-
Urothelial Carcinoma	3	2
Uterus	8	-
Other (n=1)	5	6
NOT REPORTED	2	2

**Supplementary Table 3: further analysis performed on the 29 patients with matched lbNGS, ttNGS and MTB decision.**

SAMPLE ID	FISH/PCR/IHC
A66220	<i>not performed</i>
A53203	<i>not performed</i>
A50314	<i>not performed</i>
A47277	<i>not performed</i>
A66047	<i>not performed</i>
A37300	ALK FISH (negative)
A67428	<i>not performed</i>
A56133	ALK FISH (negative)
A67475	<i>not performed</i>
A61329	<i>not performed</i>
A38346	<i>not performed</i>
A38885	<i>not performed</i>
A63641	ROS1 FISH (negative) ALK IHC (negative)
A65160	<i>not performed</i>
A67718	ROS1 FISH (negative) ALK IHC (negative)
A55662	<i>not performed</i>
A61712	ALK FISH (negative) ROS1 FISH (negative)
A38959	ALK IHC (negative) HER2 IHC (negative)
A36610	ALK FISH (negative) ROS1 FISH (negative) ALK IHC (negative)
A47888	<i>not performed</i>
A68578	<i>not performed</i>
A40228	ROS1 FISH (negative) ALK IHC (negative) HER2 (negative) PD1 (negative) PDL1 (negative)
A66216	EGFR PCR (negative)
A71123	<i>not performed</i>
A31692	ROS1 FISH (negative) ALK IHC (negative) HER2 (negative) PD1 (positive only in TILS) PD-L1 (1% in tumor, positive in TILS)
A43020	<i>not performed</i>
A61725	ALK FISH (negative) ROS1 FISH (negative) cMET FISH (negative) HER2 FISH (negative) <b>EGFR IHC (positive)</b> Negative IHCs: AR, cMET, ERCC1, ER, HER2, MGMT, PGP, PMS2, PR, PTEN, RRM1, SPARC monoclonal, SPARC polyclonal, TLE3, TOPO1, TOP2A, TUBB3, TS
A55215	<i>not performed</i>
A55224	<i>not performed</i>